
Dynamic Changes in Intracellular ROS Levels Regulate Airway Basal Stem Cell Homeostasis through Nrf2-Dependent Notch Signaling.

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Public Summary:

Airways are exposed to myriad environmental and damaging agents such as reactive oxygen species (ROS), which also have physiological roles as signaling molecules that regulate stem cell function. However, the functional significance of both steady and dynamically changing ROS levels in different stem cell populations, as well as downstream mechanisms that integrate ROS sensing into decisions regarding stem cell homeostasis, are unclear. Here, we show in mouse and human airway basal stem cells (ABSCs) that intracellular flux from low to moderate ROS levels is required for stem cell self-renewal and proliferation. Changing ROS levels activate Nrf2, which activates the Notch pathway to stimulate ABSC self-renewal and an antioxidant program that scavenges intracellular ROS, returning overall ROS levels to a low state to maintain homeostatic balance. This redox-mediated regulation of lung stem cell function has significant implications for stem cell biology, repair of lung injuries, and diseases such as cancer.

Scientific Abstract:

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